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From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

GLAWE, DELFS, MOLL & PARTNER  
Rothenbaumchausse 58  
20148 Hamburg  
ALLEMAGNE

PCT

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT

(PCT Rule 71.1)

RECEIVED INTERNATIONAL EXAMINING AUTHORITY 30 APRIL 2001		Date of mailing (day/month/year) 20.03.2001
Applicant's or agent's file reference <b>UNIXO31PEP</b>		
International application No. <b>PCT/US99/27401</b>	International filing date (day/month/year) <b>18/11/1999</b>	Priority date (day/month/year) <b>18/11/1998</b>
<b>IMPORTANT NOTIFICATION</b>		
Applicant <b>UNIVERSITY OF FLORIDA et al.</b>		

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

**4. REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  Longo, E  Tel. +49 89 2399-8141	
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## PATENT COOPERATION TREATY

## PCT

**INTERNATIONAL PRELIMINARY EXAMINATION REPORT**  
**(PCT Article 36 and Rule 70)**

Applicant's or agent's file reference <b>UNIXO31PEP</b>	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. <b>PCT/US99/27401</b>	International filing date (day/month/year) <b>18/11/1999</b>	Priority date (day/month/year) <b>18/11/1998</b>
International Patent Classification (IPC) or national classification and IPC <b>A61K9/00</b>		
Applicant <b>UNIVERSITY OF FLORIDA et al.</b>		
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of 5 sheets.</p>		
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> <li>I   <input checked="" type="checkbox"/> Basis of the report</li> <li>II   <input type="checkbox"/> Priority</li> <li>III   <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</li> <li>IV   <input type="checkbox"/> Lack of unity of invention</li> <li>V   <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</li> <li>VI   <input type="checkbox"/> Certain documents cited</li> <li>VII   <input checked="" type="checkbox"/> Certain defects in the international application</li> <li>VIII   <input checked="" type="checkbox"/> Certain observations on the international application</li> </ul>		

Date of submission of the demand <b>16/06/2000</b>	Date of completion of this report <b>20.03.2001</b>
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx. 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer <b>Rauter, A</b> Telephone No. +49 89 2399 8645



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US99/27401

**I. Basis of the report**

1. This report has been drawn on the basis of (substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).):

**Description, pages:**

1-53 as originally filed

**Claims, No.:**

1-27 as received on 19/02/2001 with letter of 16/02/2001

**Drawings, sheets:**

1/10-10/10 as originally filed

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description, pages:
- the claims, Nos.:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US99/27401

the drawings,      sheets:

5.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)): *(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. Statement**

Novelty (N)	Yes:	Claims 1 - 27
	No:	Claims
Inventive step (IS)	Yes:	Claims 1 - 27
	No:	Claims

Industrial applicability (IA)      Yes: Claims 1 - 27  
                                        No: Claims

**2. Citations and explanations  
see separate sheet****VII. Certain defects in the international application**

The following defects in the form or contents of the international application have been noted:  
**see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:  
**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

Int mational application No. PCT/US99/27401

**SECTION V. ....**

1. Reference is made to the following documents:

D1: WO-A-9 853 767

D2: WO-A-9 947 726

2. The present application satisfies the criteria set forth in Article 33(1)-(4) PCT because the subject-matter of claims 1 - 27 is new in respect of prior art as defined in the regulations (Rule 64(1)-(3) PCT), involves an inventive step (Rule 65(1)(2) PCT) and is considered industrially applicable.

D1 is concerned with a method of producing a film coating by matrix assisted pulsed laser deposition on large sensor parts. D2 discloses a method for coating a plurality of host particles with coating particles by vapour deposition, preferably laser ablation. In the latter document, TiO<sub>2</sub> or Ag targets to produce coatings on particles, such as SiO<sub>2</sub> are mentioned, however the said coatings are not biodegradable or biocompatible and there is no disclosure or suggestion that such coatings could be used for medicinal applications. There is no disclosure available which could have rendered presently claimed subject-matter obvious, in particular that medicaments (see present claim 1) could be provided which show the derived controlled drug delivery.

The formulation of claim 11, the kit of claim 22, the use of claim 24, the method of claim 25 as well as all the dependent claims comprise the new and inventive product, ie the medicament according to claim 1, and thus are considered to fulfill the requirements of Article 33(1)-(3) PCT. There exists no doubt that the claimed subject-matter is industrially applicable as required by Article 33(4) PCT.

**SECTION VII. ....**

1. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1 and D2 is not mentioned in the description, nor are these documents identified therein.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US99/27401

2. The description is not in conformity with the claims.

**SECTION VIII.....**

1. The term "about" used in the dependent claim 14 renders the defined range of the said claim vague and unclear (Article 6 PCT).
2. According to claim 2 the coating particles can be selected inter alia from cellulose "compounds", however, it appears that only "cellulose" has been originally disclosed, thus Article 34(2)(b) PCT is infringed.

PCT/US99/27401  
University of Florida  
Re/SA February 14, 2001

5

## Claims

1. A medicament comprising a plurality of coated drug particles, each having an average particle size of less than 500  $\mu\text{m}$  in diameter, the surface of said particles comprising at least a first layer of biodegradable and bio-compatible polymeric coating particles, wherein the average thickness of said coating layer is between 1 and 500 nm, the coated drug particles being obtainable through a process comprising depositing said polymeric coating particles onto the surface of host drug particles by a process comprising pulsed laser ablation.
- 20 2. The medicament according to claim 1, wherein said coating particles are selected from the group consisting of PLA, PGA, PLGA and cellulose compounds.
- 25 3. The medicament according to claim 1 or 2, wherein said drug particles have an average particle size of less than 400  $\mu\text{m}$  in diameter, preferably less than 300  $\mu\text{m}$ , further preferred less than 200  $\mu\text{m}$ , further preferred less than 100  $\mu\text{m}$ , further preferred less than 50  $\mu\text{m}$ , further preferred less than 10  $\mu\text{m}$ , further preferred less than 5  $\mu\text{m}$ , further preferred less than 1  $\mu\text{m}$ , further preferred less than 0.1  $\mu\text{m}$ .
- 30 35 4. The medicament according to any preceding claim, wherein the average thickness of said coating layer is between 1 and 400 nm, preferably 2 and 300 nm, further preferred 3

Amended claims

19-02-2001

and 200 nm, further preferred 4 and 100 nm, further preferred 5 and 50 nm.

5. The medicament according to any of the claims 1 to 3, wherein the average thickness of said coating layer is between 50 and 500 nm, preferably 100 and 500 nm, further preferred 150 and 500 nm, further preferred 200 and 500 nm, further preferred 300 and 500 nm.

10 6. The medicament according to any preceding claim, wherein the average size of the polymeric coating particles is less than 50 nm in diameter, preferably less than 40 nm, more preferred less than 30 nm, more preferred less than 20 nm, more preferred less than 10 nm, more preferred less than 5 nm.

15 7. The medicament according to any preceding claim, wherein said polymeric coating particles are applied to the surface of said drug particles to form a continuous layer.

20 8. The medicament according to any preceding claim, wherein said polymeric coating particles are applied to the surface of said drug particles to form a discontinuous layer.

25 9. The medicament according to any preceding claim, wherein said coated drug particles comprise an anti-allergic, an antibiotic, an anti-inflammatory, or a bronchodilatory drug.

30 10. The medicament according to any preceding claim, wherein said drug particles are selected from the group consist-

9-02-2001

3

ing of budesonide, triamcinolone acetonide, and rifampicin.

11. A pharmaceutical formulation comprising the medicament of  
any preceding claim.

12. The formulation according to claim 11, comprising from  
0.01 % to 10 % by weight of said medicament relative to  
the total weight of the formulation.

10

13. The formulation according to claim 11 or 12, containing  
from 0.1 % to 1 % by weight of said medicament relative  
to the total weight of the formulation.

15 14. The formulation according to any one of claims 11 to 13,  
comprising a respirable fraction of from about 20 % to  
about 50 % or more by weight of said medicament.

16. The formulation according to any of claims 11 to 13, fur-  
ther comprising a second medicament.

25 17. The formulation according to claim 15, wherein said sec-  
ond medicament comprises a medicament in accordance with  
any one of claims 1 to 10.

30 18. The formulation according to any one of claims 11 to 17,  
comprising a first bronchodilatory medicament and a sec-  
ond medicament selected from the group consisting of an  
anti-inflammatory agent, a bronchodilatory agent, an an-

tibiotic agent, and an anti-allergic agent.

19. The formulation according to any one of claims 11 to 18,  
further comprising a vehicle suitable for aerosol admini-  
stration of said formulation.

5 20. The formulation according to claim 19 further comprising  
a propellant.

10 21. The formulation according to claim 20, wherein said pro-  
pellant is selected from the group consisting of a  
fluorocarbon and a hydrogen-containing chlorofluorocar-  
bon.

15 22. A therapeutic kit comprising the medicament of any one  
of claims 1 to 10, or the formulation according to any  
one of claims 11 to 21, and instructions for the admini-  
stration of said medicament.

20 23. The therapeutic kit of claim 22, further comprising an  
aerosol delivery apparatus or a medical device suitable  
for pulmonary administration of said medicament.

25 24. The use of coated drug particles as defined in any of the  
claims 1 to 10 or of a formulation according to any of  
the claims 11 to 21 for the manufacture of a medicament  
for treating a respiratory disorder or a pulmonary infec-  
tion in a human patient.

30 25. A method of preparing coated drug particles as defined in  
any of the claims 1 to 10, the method comprising deposit-  
ing onto the surface of a host drug particle at least a

first layer that comprises a plurality of polymeric coating particles by a process comprising pulsed laser ablation under vacuum.

5        26. The method according to claim 25, wherein said pulsed laser ablation comprises a laser having a wavelength of about 240 to about 280 nm.

10        27. The method according to claim 25 or 26, wherein said pulsed laser ablation comprises a laser having a wavelength of about 248 nm.

Amended claims